DETAILED ACTION

Claims 1, 3-20, 24-27, and 30 are pending. Applicants have amended claim 9. Applicants previously cancelled claims 2, 21-23, 28-29, and 31. Claims 7-8, 11, and 17 are withdrawn from consideration as being drawn to non-elected species. **Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27, and 30 are under consideration in the instant office action.** Receipt and consideration of Applicants' amended claim set and remarks/arguments submitted on February 4, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27 21-24 and 30 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Black et al. (U.S. Patent No. 5,733,909) in view of Sakuma et al. (EP 0695544), Tanida et al. (U.S. Patent No. 6,214,378), and Faour et al. (US 2004/0204413).

Applicant Claims

Applicants claim a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) celecoxib and (b) sodium metabisulfite, present in an amount sufficient to inhibit gelatin cross-linking and/or pellicle formation in the capsule shells upon storage.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Black and Sukuma were set forth on pages 10-12 of the office action mailed on February 22, 2007. The teachings of Tanida were set forth on page 15 of the office

action mailed on February 22, 2007. Briefly, Black teaches oral pharmaceutical dosage forms (i.e. **hard or soft capsules**) comprising (i) stilbene **prodrugs of COX-2 inhibitors, which are selective for COX-2 over COX-1**, (ii) a fill material comprising water or miscible solvents (e.g. **propylene glycol, PEGs, ethanol**, etc.), and wherein aqueous suspensions of the invented formulations may contain the active in admixture with other excipients, such as **hydroxypropyl methylcellulose (HPMC), polyoxyethylene stearate, polyoxyethylene sorbitol monooleate, polyoxyethylene sorbitan monooleate (i.e. polysorbates), preservatives, coloring agents, flavoring agents, and sweetening agents** (title; abstract; col. 2, lines 45-64; col. 9, lines 15-26; col. 9, line 66 through col. 10, line 10; and col. 10, lines 35-56).

Briefly, Sukuma teaches that hard gelatin capsules are sometimes denatured (e.g. cross-linked) during storage under warmed conditions, which has been attributed to the presence of PEG and other compounds (e.g. triethyl citrate) and that this **denaturation may be minimized or prevented by the addition of free-radical scavengers in amounts of 0.01-5% w/w, preferably, such as, sodium sulfite, sodium hydrogensulfite, tocopherol, and ascorbic acid** (pg. 2, lines 21-33; abstract; pg. 2, lines 49-50; pg. 3, lines 8-17).

Briefly, Tanida teaches pharmaceutical formulations in which an active substance is encapsulated and released in the lower gastrointestinal tract. The active substance is preferably an anti-inflammatory agent that it is a COX-2 inhibitor, such as celecoxib (col. 3, lines 12-16, 41, and 56-57). Tanida's formulations may include additives, such as vehicle, liquid agent, absorbefacient, etc. (col. 3, line 62 through col. 4, line 26), wherein suitable absorbefacients include **polyethylene glycol sodium dodecyl sulfate, sucrose fatty acid esters**, etc.

Faour teaches (i) pharmaceutical compositions comprising a COX-II inhibitor (e.g. celecoxib) and a muscle relaxant (title; abstract; claims 1 and 10) and (ii) that antioxidants include **ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate, hypophosphorous acid, sodium ascorbate, sodium bisulfite, sodium metabisulfite**, etc. [0072]. Antioxidants are agents that inhibit oxidation and are also known as free-radical scavengers.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Black lacks the teaching of pharmaceutical dosage forms comprising sodium metabisulfite. This deficiency is cured by the teachings of Faour.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Black/Sukuma and Tanida, because the Black/Sukuma combination teaches capsule formulations comprising a selective COX-2 inhibitor and Tanida teaches capsule formulations wherein it is preferable to utilize a COX-2 inhibitor as an anti-inflammatory agent. A person of ordinary skill in the art would have been motivated to either substitute celecoxib for Black's invented selective COX-2 inhibitors or include celecoxib as an additional active agent because Black teaches that additional active agents may be included in the composition. Furthermore, the inclusion of an additional selective COX-2 inhibitor having a different core structure would be expected to at least yield an additive

effect regarding the compositions' ability to inhibit COX-2 and therefore an ordinary skilled artisan would have had a reasonable expectation of success. Regarding the possibility of substitution of celecoxib for Black's invented COX-2 inhibitors, an ordinary skilled artisan would have had a reasonable expectation of success because celecoxib is a known selective COX-2 inhibitor. Faour's teachings demonstrate that sodium sulfite and sodium metabisulfite are functional equivalents. Thus, given Sakuma' preference for the inclusion of sulfite compounds and the fact that sodium sulfite and sodium metabisulfite are functional equivalents, it would have been prima facie obvious to substitute sodium metabisulfite for sodium sulfite or to add sodium metabisulfite to a composition comprising sodium sulfite, because an ordinary skilled artisan would have had a reasonable expectation of success upon substitution or inclusion of sodium metabisulfite in the compositions of the combined prior art references. Regarding the inclusion of sodium metabisulfite in the fill material in addition to inclusion in the gelatin capsule, this would have been prima facie obvious because sodium metabisulfite would reasonably be expected to offset any oxidation that may denature the gelatin capsule in physical contact with the fill material contained within said capsule. Furthermore, Applicants' data does not demonstrate any surprising or unexpected results, because free radical scavengers (i.e. antioxidants), such as sodium sulfite and sodium metabisulfite, were known to prevent gelatin oxidation/denaturation. Applicants' data do not demonstrate any criticality to the presence of sodium metabisulfite only being found in the fill material as opposed to being admixed with the gelatin capsule or being both admixed with the capsule material and fill material. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in

the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed 2/4/2008 have been fully considered but they are not persuasive. Applicants have traversed the instant rejection by arguing that the office has allegedly not made prima facie showing of obviousness and alleging that "none of the cited references describe a dosage form comprising a fill material sealed in capsule shells wherein the fill material comprises celecoxib and sodium metabisulfite.

The Examiner respectfully disagrees with Applicants' traversal argument, because the Office has made a prima facie showing of obviousness. Applicants' arguments are deemed as an attack of the cited references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, it is noted that the combined teachings of the prior art, teach pharmaceutical dosage forms comprising a fill material sealed in capsules, wherein said fill material comprises celecoxib (Tanida) and sodium metabisulfite (Faour). It is also noted that the prior art recognized that gelatin capsules were susceptible to cross-linking and pellicle formation and that the prior art recognized that the inclusion of antioxidants, such as sodium sulfite and sodium hydrogensulfite, in amounts ranging from 0.01-5% w/w is sufficient to inhibit or prevent pellicle formation (Sukuma). The art recognizes that sodium metabisulfite is an antioxidant. Thus, the

substitution of one known antioxidant for another is obvious and would reasonably be expected to inhibit or prevent pellicle formation in gelatin capsules. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention and the instant rejection remains proper.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejections on the ground of nonstatutory obviousness-type double patenting of claims 1, 4, 10, and 24 as being unpatentable over claims 19-20, 23, and 32-33 of copending Application No. 10/633,194 (copending '194) **is maintained** for the reasons of record which are restated below and because Applicants have not traversed the instant rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because these are substantially overlapping in scope and mutually obvious. Independent claim 1 of the instant application has been described *supra*. Dependent claim 6 of copending '390 claims a pharmaceutical dosage form comprising a fill material sealed in capsule shells wherein said fill material comprises (a) a selective low water solubility COX-2 inhibitor, (b) an amine agent; and (c) at least one sulfite compound. As discussed above, the use of comprising language in both applications allows for the presence of additional unnamed excipients and/or active materials in the claimed dosage form. For these reasons, the Examiner concludes that the cited claims of the instant application are *prima facie* obvious over the cited claims of copending '390.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Other Matter

It is noted that the status of claim 17 as being previously presented is not completely accurate, because claim 17 was withdrawn from consideration as of the office action mailed on February 22, 2007.

Conclusion

Claims 1, 3-6, 9-10, 12-16, 18-20, 24-27, and 30 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616